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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

AUG 27 1993

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: **Bromoxynil Octanoate.** Sorghum Crop Field Trials. Reregistration Case No. 2070. Chemical No. 035302. MRID #42718702. DP Barcode D190384. CBRS #11,754.

FROM: Steven A. Knizner, Chemist
Special Review Section I
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Health Effects Division (H7509C)

THRU: Edward Zager, Chief
Chemistry Branch II - Reregistration Support
Health Effects Division (H7509C)

TO: Thomas Luminello, Jr., PM Team 52
Special Review and Reregistration Division (H7508W)

The Bromoxynil Phase 4 Review (L. Cheng, dated 1/30/91) identified magnitude of the residue data gaps for sorghum crop field trials. In response, Rhone-Poulenc Ag Co. (1993; MRID 42718702) submitted magnitude of residue data for sorghum grain, forage (including freshly cut silage), fodder, and hay. These data have been reviewed by Acurex Corp., and have undergone secondary review in CBRS to reflect Branch policies.

Crop treatments used in field trials do not accurately reflect label directions. If the registrant wishes to retain the chemigation application and a maximum seasonal application of 0.75 lb ai/A, additional field trials are required. The field trials should be conducted in IL, SD, CO, and NC/GA.

Above tolerance residues were detected in sorghum forage and fodder. No tolerances exist for sorghum hay, but residues of up to 0.45 ppm were detected. Please see Conclusion 2 in the attachment for details on the levels of residues found.

Regarding over-tolerance bromoxynil residues in or on sorghum raw agricultural commodities, the following options are open to the registrant: 1) Propose new tolerances of for sorghum forage at 0.5 ppm, fodder at 0.2 ppm, and hay at 0.5 ppm; or 2) Amend all registered labels to include a 45 day feeding/grazing interval, and propose new tolerances for

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sorghum fodder at 0.2 ppm and hay at 0.1 ppm (current forage tolerance will remain acceptable).

In addition to the changes in tolerances, all product labels must be amended to permit a single application at up to 0.5 lb ai/A/season, and unless additional data are provided, the chemigation application pattern must be removed from the label.

If you need additional input please advise.

Attachment.

cc: S.F., circ., R.F., List B File, S.Knizner, ACUREX
RDI: M.Metzger, 8/27/93
H7509C:CBRS:CM#2:305-6903:SAK:sak:Bromox.sor:8/25/93

BROMOXYNIL
(Chemical Codes 035301, 035302, and 128920)
(CBRS No. 11754; DP Barcode D190384)

TASK 2B

Phase 5 - Reregistration Review
Residue Chemistry

June 24, 1993

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

Acurex Environmental Corporation
Eastern Regional Operations
4915 Prospectus Drive
P.O. Box 13109
Research Triangle Park, NC 27709

BROMOXYNIL

(Chemical Codes 035301, 035302, and 128920) (CBRS No. 11754; DP Barcode D190384)

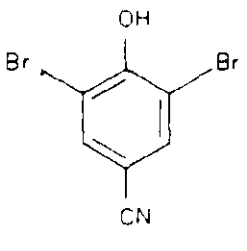
BACKGROUND

The Bromoxynil Phase 4 Review (L. Cheng, dated 1/30/91) identified magnitude of the residue data gaps for sorghum crop field trials. In response, Rhone-Poulenc Ag Co. (1993; MRID 42718702) submitted magnitude of residue data for sorghum grain, forage, silage, fodder, and hay. Overtolerance residues were found in or on at least three treated samples of each matrix except grain. These data are reviewed here for adequacy in fulfilling outstanding residue chemistry requirements. The Conclusions and Recommendations stated in this review pertain only to the magnitude of bromoxynil residues in or on sorghum grain, forage, and fodder.

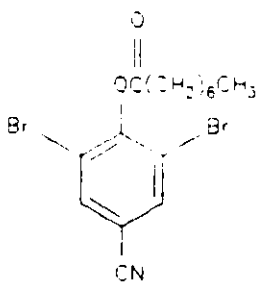
The qualitative nature of the residue in plants and animals is not adequately understood. The registrant has committed to submit the requisite data. The Phase 4 review concluded that Method B in PAM, Vol. II (which uses boron trifluoride/methanol rather than diazomethane in the derivatization reaction) is adequate for enforcing tolerances for currently known bromoxynil residues in plant commodities.

Tolerances of 0.1 ppm are currently established in or on numerous RACs, including those subject to this review, for residues of the herbicide bromoxynil (3,5-dibromo-4-hydroxybenzonitrile) resulting from application of the phenol per se, or its octanoic, butyric, and heptanoic acid esters [40 CFR §180.324(a), (b), and (c)]. The Phase 3 submission indicated that products containing the heptanoic and butyric acid esters of bromoxynil would not be supported through reregistration, which was confirmed in the 90-day response to the Phase 4 DCI. However, Rhone-Poulenc Ag Co. has registered a product containing the heptanoic acid ester [EPA Reg. No. 264-531, registered 2/25/93 (REFS search dated 6/1/93)]. CBRS has recommended that 40 CFR §180.324 be revised to combine the tolerances under sections (a)-(c) under a single tolerance expression stated as the herbicide bromoxynil (3,5-dibromo-4-hydroxybenzonitrile) resulting from application of its octanoic and/or heptanoic acid esters (C. Swartz; CBRS Nos. 8665 and 8667, 1/21/92).

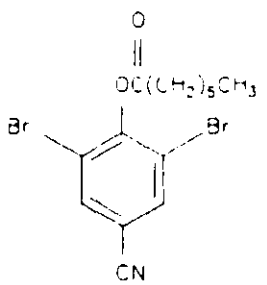
No Codex MRLs have been established for residues of bromoxynil; therefore, there is no question regarding compatibility with U.S. tolerances.



Bromoxynil



Bromoxynil Octanoate



Bromoxynil Heptanoate

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RECOMMENDATIONS

Regarding over-tolerance bromoxynil residues in or on sorghum raw agricultural commodities, the following options are open to the registrant: 1) Propose new tolerances for sorghum forage at 0.5 ppm, fodder at 0.2 ppm, and hay at 0.5 ppm; or 2) Amend all registered labels to include a 45 day feeding/grazing interval, and propose new tolerances for sorghum fodder at 0.2 ppm and hay at 0.1 ppm (current forge tolerance will remain acceptable).

In addition to the changes in tolerances, all product labels must be amended to permit a single application at up to 0.5 lb ai/A/season, and unless additional data are provided, the chemigation application pattern must be removed from the label.

CONCLUSIONS

1. Crop treatments used in field trials do not accurately reflect label directions (see Table 2). For all field trials, a single post-emergence treatment at 0.5 lb ai/A using ground or aerial equipment was made. All bromoxynil labels permit a maximum ground/aerial application rate of 0.375 lb ai/A/application. All bromoxynil labels specify a maximal seasonal application limit of 0.75 lb ai/A/season. None of the field trials reflected the maximum seasonal application rate. This is a deficiency. Although required by the Phase 4 Review, no trials reflecting chemigation application of bromoxynil at 0.5 lb ai/A were made. This is a deficiency. If the registrant wishes to retain the chemigation application and a maximum seasonal application of 0.75 lb ai/A, additional field trials are required. The field trials should be conducted in IL, SD, CO, and NC/GA.

2. **Above tolerance residues were detected in sorghum forage and fodder. No tolerances exist for sorghum hay, but residues of up to 0.45 ppm were detected.**

2.a. Sorghum Forage Overtolerance residues (0.11-0.29 ppm) of bromoxynil were found in or on samples collected 29-31 days posttreatment in 7 of 14 field trial locations. Residues were 0.02-0.10 ppm in or on samples collected 30-31 days posttreatment in the other 7 locations (see Table 3). Forage samples collected 45 days posttreatment had bromoxynil residues ranging from <0.02 to 0.09 ppm.

2.b. Sorghum Fodder Overtolerance residues of bromoxynil (0.12-0.14 ppm) were found in or on fodder samples harvested 107 days posttreatment at the TX site; residues were <0.02-0.08 ppm in or on the remaining treated samples from the 12 other test locations (grain and fodder samples were not collected from one of the KS sites) harvested 64-94 days posttreatment. The registrant must discuss the high residue levels found for the TX test (test number 91-228), and indicate whether anomalies

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occurred during application or at any other stage of the field test that could have led to excessive residues in the fodder.

2.c. Sorghum Hay Residues of bromoxynil were <0.02-0.45 ppm in or on hay samples from 6 locations harvested 29-31 days posttreatment, and were 0.03-0.07 ppm in or on samples from 8 locations harvested 43-46 days posttreatment (Table 3). The data indicate that a tolerance of 0.5 ppm should be proposed for residues of bromoxynil in or on sorghum hay, with a 30 day PHI; or a tolerance of 0.1 ppm with a 45 day PHI.

2.d. Sorghum Silage There are no tolerances for bromoxynil in or on sorghum silage. Residues were <0.02-0.09 ppm in or on treated samples from the 14 locations collected 42-107 days posttreatment (Table 3).

2.e. Sorghum Grain Residues of bromoxynil were <0.02 ppm (< LOQ) in or on all analyzed grain samples (13 sites, grain and fodder samples were not collected from one of the KS sites) harvested 64-107 days after application (Table 3).

3. All previous storage stability data requirements remain outstanding. In addition, the registrant must document its statement in the current submission concerning sample storage temperatures exceeding protocol in sufficient detail to allow the Agency to determine whether sample integrity was compromised. The registrant must also fully document, in detail, the storage history for all forage samples collected at the silage (hard dough) stage, including sample condition, storage temperatures (minimum and maximum), and sample handling at each step from collection through analysis (including shipping). Summary tables and good quality exact photocopies of freezer temperature charts may be included to supplement the discussion.

4. The submitted residue analytical method data adequately support the current residue analyses. If the outstanding metabolism studies identify additional residues of concern, additional residue analytical methodology, storage stability, and magnitude of residue data will be required.

DETAILED CONSIDERATIONS

Residue Analytical Methods

In conjunction with the residue study, Rhone-Poulenc Ag Co. (1993; MRID 42718702) submitted descriptions of a modified GC/ECD method (SOP No. 90020). Using the modified method, residues are extracted by boiling the sample matrix under reflux with 1N methanolic KOH, and cleaned up using anionic exchange resin. The residues are extracted from the resin into 15% ether in hexane by acidifying with 1N HCl and 1N KCl (50:50 v:v). Residues in the organic phase are concentrated, methylated using diazomethane, and

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quantified as bromoxynil methyl ether using GC/ECD. Modifications included omitting an optional silica gel clean up following methylation, and employing dual-column separation (a DB 1701 column connected to a DB-5 column) during analyses of most of the treated samples to enhance separation of bromoxynil methyl ether from interfering peaks. The method limits of detection (LOD) and quantitation (LOQ) for bromoxynil methyl ether were reported to be 0.01 ppm and 0.02 ppm, respectively, for each matrix.

Method validation recoveries are shown in Table 1. Concurrent method recoveries were consistent between single- and dual-column analyses, and are summarized along with the residue data in Table 2. Apparent residues of bromoxynil were <0.02 ppm ($<$LOQ) in or on a control sample of each matrix analyzed concurrently with the method validation fortifications. Representative chromatograms were provided.

Table 1. Method validation recoveries from sorghum RACs fortified with bromoxynil octanoate (two samples per matrix per fortification level).

Matrix	% Recovery at fortification level (ppm)		
	0.02	0.1	1
Grain	73, 100	79, 82	107, 96
Forage	85, 116	80, 76	96, 90
Silage	83, 88	86, 105	98, 78
Fodder	75, 85	84, 108	90, 90
Hay	66, 99	88, 86	90, 96

The submitted residue analytical method data adequately support the current residue analyses. If the outstanding metabolism studies identify additional residues of concern, additional residue analytical methodologies will be required.

Storage Stability Data

The registrant has committed to submit storage stability data; however, no storage stability studies have been submitted to date. In the current study, treated samples were stored frozen ($\leq$ -8 °C prior to shipping from the field cooperators via overnight air express or freezer truck; at approximately -10 °C at the registrant's facilities; at approximately -20 °C at the analytical laboratory) for up to 437 days (grain), 481 days (forage), 433 days (fodder), and 475 days (hay) from time of sampling until extraction for analysis.

The registrant reported that "all samples were stored frozen except during analysis, but that there were short periods of time when storage temperatures were higher than recommended in the protocol." However, the registrant did not elaborate on this general statement, nor

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were protocol deviations reported to indicate which treated samples were affected. In addition, the registrant noted that 6 silage samples (more specifically, forage samples harvested at the silage stage) had partially molded prior to analysis, and that one of these was completely moldy and therefore no portion of it was analyzed.

Storage stability data are required to support the current residue analyses. In addition, the registrant must document its statement concerning sample storage temperatures exceeding protocol, in sufficient detail to allow the Agency to determine whether sample integrity was compromised. The registrant must also fully document, in detail, the storage history for all forage samples collected at the silage stage, including sample condition, storage temperatures (minimum and maximum), and sample handling at each step from collection through analysis (including shipping). Summary tables and good quality exact photocopies of freezer temperature charts may be included to supplement the discussion.

Magnitude of the Residue in Plants

Field Trials

Rhone-Poulenc Ag Co. (1993; MRID 42718702) submitted data from 14 tests conducted in AR (1), OK (1), TX (2), MO (3), NE (3) and KS (4), the number of sites per state is in parentheses. The test states of AR (3%), KS (32%), MO (7%), NE (19%), OK (3%), and TX (24%) accounted for approximately 88% of the 1990 U.S. sorghum production (Agricultural Statistics 1991, p. 52). Although the Phase 4 Review required that studies also be conducted in IL, SD, CO, NC/GA, CBRS concludes that geographic representation for is adequate.

Application

A REFS search dated 6/1/93 listed three products registered for use on sorghum, two EC formulations [EPA Reg. Nos. 264-437 (1 lb/gal) and 264-477 (2 lb/gal); octanoic acid ester)] and a recently registered 28.7% WP formulation (EPA Reg. No. 264-531; mixed heptanoic/octanoic acid esters; registered 2/25/93). Use directions for these products on sorghum, according to most recently Agency approved label are summarized in Table 2.

Table 2. Summary of use directions for products containing bromoxynil as ai on sorghum.

Date Label Approved	EPA Reg. No.	Formulation	Application Type	Max. Rate per Application (lb ai/A)	Max. Seasonal Rate (lb ai/A)	Grazing/ Feeding Restriction
8/31/92	264-437	EC 2 lb ai/gal	Aerial/Ground	0.375	0.75	30 days
			Chemigation	0.5	0.75	30 days
5/21/92	264-477	EC 1 lb ai/gal	Aerial/Ground	0.375	0.75	30 days
2/25/93	264-531	27.7% WP	Aerial/Ground	0.375	0.75	30 days

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For all field trials, a single post-emergence treatment of Buctril (EPA Reg. No. 254-437, 2EC formulation) at 0.5 lb ai/A in 15-20 gal/A using ground equipment (11 tests) or 3.5-5 gal/A using aerial equipment (3 tests) was made. As can be seen in Table 2, all bromoxynil labels permit a maximum ground/aerial application rate of 0.375 lb ai/A/application. Therefore, all field trials were conducted at an exaggerated rate (1.33X) for a single application.

All bromoxynil labels have a seasonal application limit of 0.75 lb ai/A/season. None of the field trials reflected the maximum seasonal application rate. This is a deficiency.

Although required by the Phase 4 Review, no trials reflecting chemigation application of bromoxynil at 0.5 lb ai/A were made. This is a deficiency.

If the registrant wishes to retain the chemigation application and a maximum seasonal application of 0.75 lb ai/A, additional field trials are required. The field trials should be conducted in IL, SD, CO, and NC/GA. Protocols for these trials should be submitted to the Agency for review.

Results

Above tolerance residues were detected in sorghum forage and fodder. No tolerances exist for sorghum hay, but residues of up to 0.45 ppm were detected.

Sorghum Forage Tolerances of 0.1 ppm have been established for residues of bromoxynil resulting from the application of the phenol or its butyric, heptanoic, or octanoic acid esters in or on sorghum forage [40 CFR §180.324(a)-(c)].

Four forage samples (three treated and one control) were collected 29-31 days posttreatment from all sites. All samples were frozen after collection and were stored at ≤ -8 °C prior to shipment to the registrant's facilities via overnight air carrier or freezer truck. Samples were stored frozen for 312-481 days from time of sampling until extraction for analysis using the modified GC/ECD method SOP No. 90020.

Overtolerance residues (0.11-0.29 ppm) of bromoxynil were found in or on samples from 7 of 14 locations collected 29-31 days posttreatment. Residues were 0.02-0.10 ppm in or on samples from the other 7 locations collected 30-31 days posttreatment (see Table 3; tests with overtolerance residues are individually presented and shaded). Forage samples collected with a 45 day PHI had bromoxynil residues ranging from <0.02 to 0.09 ppm. Only 12 forage samples with a 45 day PHI were analyzed; because samples from AR (1) and KS (1) had reached the silage (hard dough) stage by this time they were not analyzed.

Apparent residues of bromoxynil were <0.02 ppm (<LOQ) in or on all 14 untreated forage control samples. Concurrent method recoveries were 74-04% from 14 forage controls

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fortified with bromoxynil octanoate at 0.1 ppm, 100% from a control fortified at 0.5 ppm, and 99% from a control fortified at 0.05 ppm. Residues found in or on treated forage samples were not corrected for concurrent method recoveries.

Sorghum Fodder Tolerances of 0.1 ppm have been established for residues of bromoxynil resulting from the application of the phenol or its butyric, heptanoic, or octanoic acid esters in or on sorghum fodder [40 CFR §180.324(a)-(c)].

Four fodder samples per site (three treated and one control) were collected at grain harvest, and were stored at ≤ -8 °C prior to shipment to the registrant's facilities via overnight air carrier or freezer truck. Samples were stored frozen for 304-433 days from time of sampling until extraction for analysis using the modified GC/ECD method SOP No. 90020.

Overtolerance residues of bromoxynil (0.12-0.14 ppm) were found in or on three treated fodder samples harvested 107 days posttreatment at the TX site; residues were <0.02-0.08 ppm in or on the remaining 36 treated samples (grain and fodder samples were not collected from one of the KS sites) harvested 64-94 days posttreatment (Table 3).

Apparent residues of bromoxynil were <0.02 ppm (<LOQ) in or on each fodder control. Concurrent method recoveries were 74-104% from 13 control samples fortified at 0.1 ppm with bromoxynil octanoate. Residues found in or on treated fodder samples were not corrected for concurrent method recoveries.

The registrant must discuss the high residue levels found for the TX test (test number 91-228), and indicate whether anomalies occurred during application or at any other stage of the field test that could have led to excessive residues in the fodder.

Sorghum Hay No tolerances for residues of bromoxynil have been established for sorghum hay.

Four hay samples (three treated and one control) were collected 29-31 days posttreatment from all sites, and were collected 43-46 days posttreatment from 8 of the 14 sites. After harvest, hay samples were allowed to dry at ambient temperature (in the field, or indoors in mesh bags, on drying racks, or using forced air) for 2-6 days or an unspecified interval. Following drying, samples were frozen at ≤ -8 °C prior to shipment to the registrant's facilities via overnight air carrier or freezer truck. Samples were stored frozen for approximately 337-475 days from time of sampling until extraction for analysis using the modified GC/ECD method SOP No. 90020.

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Residues of bromoxynil were <0.02-0.45 ppm in or on hay samples from 6 locations harvested 29-31 days posttreatment, and were 0.03-0.07 ppm in or on samples from 8 locations harvested 43-46 days posttreatment (Table 3). Apparent residues of bromoxynil were <0.02 ppm (<LOQ) in or on 15 of 22 hay controls, and were 0.02-0.04 ppm in or on 7 hay control samples. Concurrent method recoveries were 70-115% from 22 hay controls fortified with bromoxynil octanoate at 0.1 ppm (21 samples) or 0.2 ppm (1 sample). Residues found in or on treated hay samp'es were not corrected for concurrent method recoveries.

The data indicate that a tolerance of 0.5 ppm should be proposed for residues of bromoxynil in or on sorghum hay, with a 30 day PHI.

Sorghum Silage There are no tolerances for bromoxynil in or on sorghum silage. Silage samples were collected when the sorghum reached the hard dough stage (43-107 days posttreatment). Residues were <0.02-0.09 ppm in or on treated samples from the 14 locations collected 42-107 days posttreatment (Table 3). One treated sample was not prepared for analysis because the analytical laboratory reported it to be completely moldy. An additional five samples were reported to be partially moldy; the moldy portions were removed prior to analysis.

Sorghum Grain Tolerances of 0.1 ppm have been established for residues of bromoxynil resulting from the application of the phenol or its butyric, heptanoic, or octanoic acid esters in or on sorghum grain [40 CFR §180.324(a)-(c)].

Residues of bromoxynil were <0.02 ppm (<LOQ) in or on all treated grain samples (13 sites, grain and fodder samples were not collected from one of the KS sites) harvested 64-107 days after application (Table 3). Four mature grain samples per site (three treated and one control) were frozen following harvest, and were stored at ≤ -8 °C prior to shipment to the registrant's facilities via overnight air carrier or freezer truck. Samples were stored frozen for 298-437 days from time of sampling until extraction for analysis using the modified GC/ECD method SOP No. 90020. Apparent residues of bromoxynil were also <0.02 ppm in or on each grain control. Concurrent method recoveries were 74-111% from 15 control samples fortified at 0.1 ppm (12 samples) or at 0.02 ppm (3 samples) with bromoxynil octanoate. Residues found in or on treated grain samples were not corrected for concurrent method recoveries.

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Table 3. Residues of bromoxynil found in or on treated sorghum grain, forage (including freshly cut silage), fodder, and hay.

Commodity	Test information[a]	Posttreatment interval (days)	Residues found (uncorrected ppm)	Concurrent method recovery[b] (%)	Storage interval (days)
Grain	13 of 13 test locations[c]	64-107	<0.02	74-111	298-437
Forage	7 of 14 test locations	30-31	0.02-0.10	74-104	374-481
	OK (90-001)	29	0.19, 0.23, 0.29	100	377
	KS (91-172)	30	0.06, 0.22, 0.27	100	377
	KS (91-173)	30	0.12, 0.13, 0.17	78	366
	KS (91-174)	30	0.05, 0.08, 0.22	97	358
	TX (91-228)	30	0.13, 0.13, 0.19	78	383
	MO (91-274)	30	0.09, 0.11, 0.18	78	371
	MO (91-275)	30	0.11, 0.12, 0.15	89	389
	12 of 12 test locations	45	<0.02-0.09	78-116	361-446
Fodder	12 of 13 test locations	64-94	<0.02-0.08	74-104	304-433
	TX (91-228)	107	0.12, 0.13, 0.14	84	320
Silage	14 of 14 test locations	43-107	<0.02-0.09	78-116	338-434
Hay	8 of 14 test locations	30-31	0.03-0.10	76-109	358-475
	OK (90-001)	29	0.05, 0.10, 0.12	80	347
	NE (91-147)	31	0.02, 0.06, 0.12	115	389
	KS (91-172)	30	0.08, 0.20, 0.33	70	412
	KS (91-173)	30	0.09, 0.14, 0.15	86	365
	KS (91-174)	30	0.12, 0.17, 0.24	89	391
	TX (91-228)	30	0.15, 0.36, 0.45	80	370
	8 of 8 test locations[d]	43-46	<0.02-0.07	72-96	337-474

[a]Tests with residues exceeding the established 0.1 ppm tolerance for sorghum grain, forage, and fodder are individually presented and shaded. [b]All but a few of the concurrent method recovery samples were fortified at 0.1 ppm; see text for fortification levels and number of samples fortified at each level. [c]Grain and fodder samples were not harvested from one KS test. [d]Hay samples were not collected at the 45-day posttreatment target interval from 6 locations because the grain had matured to the silage stage.

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References

Citations for the MRID documents references in this review are presented below. Submissions reviewed in this document are indicated by shaded type.

42718702 Cappy, J. (1993) BUCTRIL/Sorghum/Magnitude of Residue: Lab Project Number: USA91203: 44109. Unpublished study prepared by McKenzie Lab., Inc. 360 p.

Agency memoranda

CBRS Nos. 8665 and 8667
Subject: Rhone-Poulenc Ag Co. Phase 4 DCI 90-Day Response.
From: C. Swartz
To: L. Deluise
Dated: 1/21/92
MRID(s): n/a

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